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Amphiphilic Linear-branched Copolymers and Their Fluorinated Dendritic Analogs

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Introduction

Amphiphilic copolymers are being considered for a number of applications such as surfactants, coatings, adhesives, and drug delivery systems. Convergent polyether dendrimers¹ are known to have significant hydrophobic character while poly(ethylene glycol) (PEG) is a typical hydrophilic polymer. In our group, these two types of macromolecules have been combined together to form amphiphilic copolymers with a unique macromolecular architecture, a hybrid of linear and branched structures^{2,4}. These copolymers, either ABA triblock copolymers or 4-arm star copolymers, have shown interesting properties in different solvents such as THF, CHCl₃, MeOH or MeOH/water. The amphiphilic materials respond to the changed polarity of different solvents and self-assemble to adopt different conformations. For example, they adopt a fully extended structure in CHCl₃, while in MeOH the dendritic components collapse to form a hydrophobic core surrounded by PEG; finally, in THF the copolymers minimize their free-energy by forming a tight PEG core surrounded by dendritic arms extending outwards.

If the properties of such a branched-linear structure are related to its overall architecture rather than exact structural features, the regular dendritic components might be replaced by simpler branched structures with similar hydrophobicity. In this paper, we explore the design of simple branched molecules that might be used to replace the dendritic components in these hybrid macromolecules. We also explore changes in hydrophobicity of the hybrid macromolecules obtained by attaching fluorinated chains to the dendrimer periphery. In comparison to the normal hydrocarbon dendrimers, the fluorinated branched moieties that are wrapped with PEG will tend to be more compact in hydrophilic polar solvents. This fluorinated copolymer is expected to exhibit interesting micelle forming characteristics and other solution properties.

Experimental

Materials. Poly(ethylene glycol)s (PEGs) with narrow polydispersities were purchased from Scientific Polymer Products, Inc. 4-arm star PEG was purchased from Shearwater Polymers, Inc. THF was dried prior to use. Other chemicals were obtained from Aldrich and used as received.

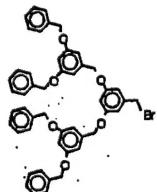
Synthesis of copolymers of PEG and dendrimers. The synthesis of copolymers of polyether dendrimer and PEG has been reported previously². The fluorinated dendrimer reacted with PEG diol under a similar condition. PEG diol ($M_n = 4200$, PDI = 1.05) and fluorinated dendrimer F₂₅-[G-2]-Br (2.1 equiv.) were dissolved in dry THF. Large excess of NaH was added at once to the solution at room temperature. After 6 hrs, the remained NaH was filtered and the filtrate was precipitated into acetone/ether (1/4). The light yellow polymer was collected and dried.

Synthesis of copolymers of PEG and dendritic analogs. The syntheses of dendritic analogs are shown in Scheme 1 and 2. PEG(CDI)₂ was synthesized according to the published procedure⁵. PEG(CDI)₂ and 2.5 equivalents of dendritic analogs (either compound 4 or 5) were dissolved in a mixture of THF/CH₃CN. AgF (3 equiv.) was added and the reaction mixture was heated to 70 °C for 4 hrs. The resulting polymer was purified following the same procedure described above.

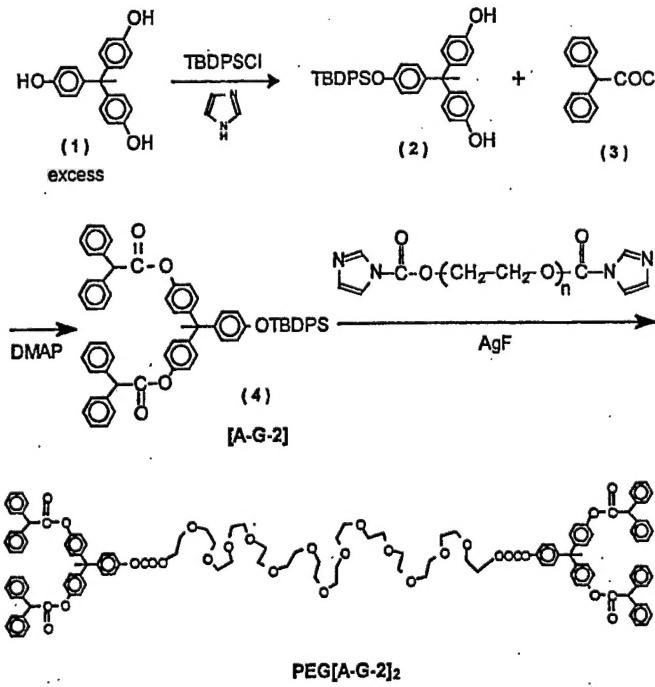
Characterization. The copolymers were characterized using NMR, GPC, MALDI-TOF mass spectrometry and contact angle measurements.

Results and Discussion

I. Copolymers of PEG and branched analogs of dendrimers.



Since a typical second-generation dendrimer ([G-2]-Br) used in the synthesis of PEG-dendrimer copolymer bears 7 aromatic rings as shown above, we designed the branched analogs to have a similar chemical structure to the normal second-generation dendrimer. The first synthesis of such a branched analog of dendrimer [A-G-2] is depicted in Scheme 1. The dendrimer and its analogs have several characteristics in common, i.e., seven aromatic rings, same numbers of branching and similar molecular weights, and importantly they are all hydrophobic. The branched analog was prepared using commercially available cheap starting materials in a straightforward synthesis. An initial attempt to attach two equivalents of diphenylacetyl chloride to 1,1,1-tris(4-hydroxyphenyl ethane) failed as the tri-functionalized compound was isolated. Bifunctional compound 4 [A-G-2] was obtained after protecting one of the phenolic groups in a reaction involving a large excess of 1,1,1-tris(4-hydroxyphenyl ethane) with respect to tert-butyldiphenylsilyl chloride (TBDPSCl). Excess compound 1 can easily be recovered after reaction. PEG was activated by 1,1'-carbonyldiimidazole (CDI). In order to avoid an additional deprotection step, the silyl protecting group was used since the protected compound 4 can be used directly in the final coupling step without deprotection. Figure 1 shows the MALDI-TOF mass spectra of the various polymers: PEG[A-G-2]₂, the original PEG, activated PEG (PEG(CDI)₂), and the copolymer of PEG and dendrimer (PEG[G-2]₂). The average molecular weights can be measured based on the spectra and the differences between the polymers and the original PEG match the molecular weight of each component added to the PEG. The MALDI-TOF spectra of the two copolymers indicate that they have similar molecular weights. For each spectrum, the mass difference between two adjacent peaks is 44 daltons, a value that corresponds to the molecular weight of the repeat unit of PEG. The NMR spectra show the same trend for both PEG[A-G-2]₂ and PEG[G-2]₂: in THF and CHCl₃, the peaks corresponding to the aromatic moieties are sharp while the peaks become much broader in a polar solvent such as MeOH. This can be explained by different conformations achieved in THF, CHCl₃ and MeOH. In MeOH, the hydrophobic dendrimers or their analogs are surrounded by flexible PEG long chains so that the protons on the branched aromatic portion are shielded and their NMR signals become broader.



Scheme 1. Preparation of analog of [G-2] dendrimer and its copolymer with linear poly(ethylene glycol).

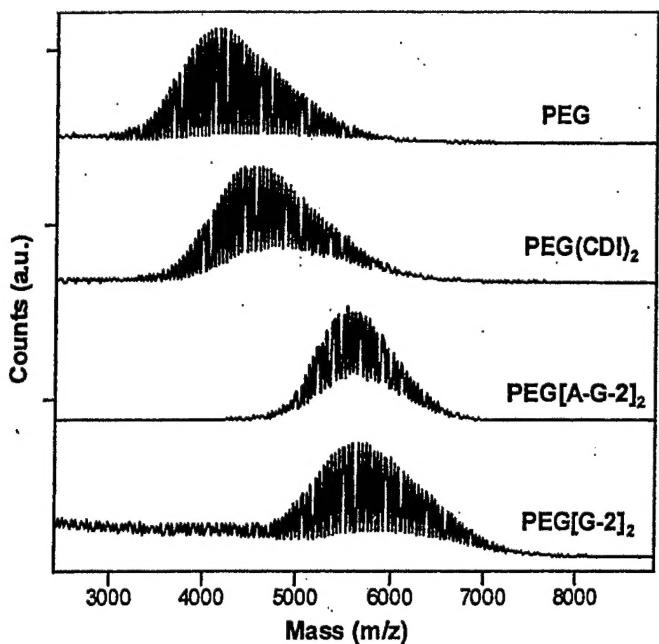
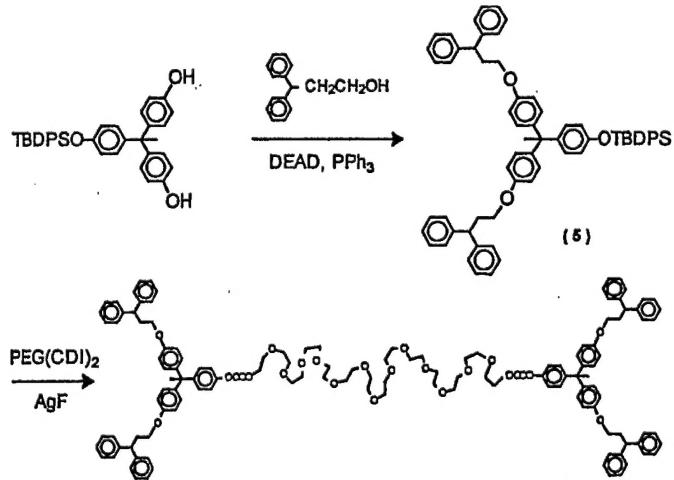


Figure 1. MALDI-TOF mass spectra of original poly(ethylene glycol); activated PEG: PEG(CDI)₂; copolymer of dendrimer analog and PEG: PEG[A-G-2]₂; copolymer of dendrimer and PEG: PEG[G-2]₂.

Because the ester groups in the analog of dendrimer are not as stable as ether linkages, their replacement by ether linkages can be accomplished via a Mitsunobu reaction using a less hindered primary alcohol (Scheme 2). In addition, we are also exploring alternative, readily accessible, branched structures that may replace dendrimers in such applications.



Scheme 2. Preparation of a dendrimer analog with ether linkages and its triblock copolymer with PEG.

II. Fluorinated copolymers.

Dendrimers with flexible fluorinated alkyl chains have been prepared according to ref. 6. Two types of copolymers have been prepared using the Williamson ether synthesis to form either dumbbell or 4-arm star structures (Figure 2). The copolymers have been characterized by ¹H, ¹⁹F NMR and MALDI-TOF mass spectrometry. The contact angle measurement for the dumbbell shows that the equilibrium contact angle is 67 degrees, the advancing contact angle is 72°, and receding contact angle is 32° if

hexadecane is used as the test liquid. Water is not a good test fluid for this measurement as it interacts strongly with the PEG portion of the copolymers. The 4-arm star copolymer gave similar results. NMR spectra in MeOH show even broader peaks in the aromatic region than is the case for the non-fluorinated analog copolymer. The properties of this fluorinated copolymer will be further studied by light scattering and small angle neutron scattering (SANS) techniques.

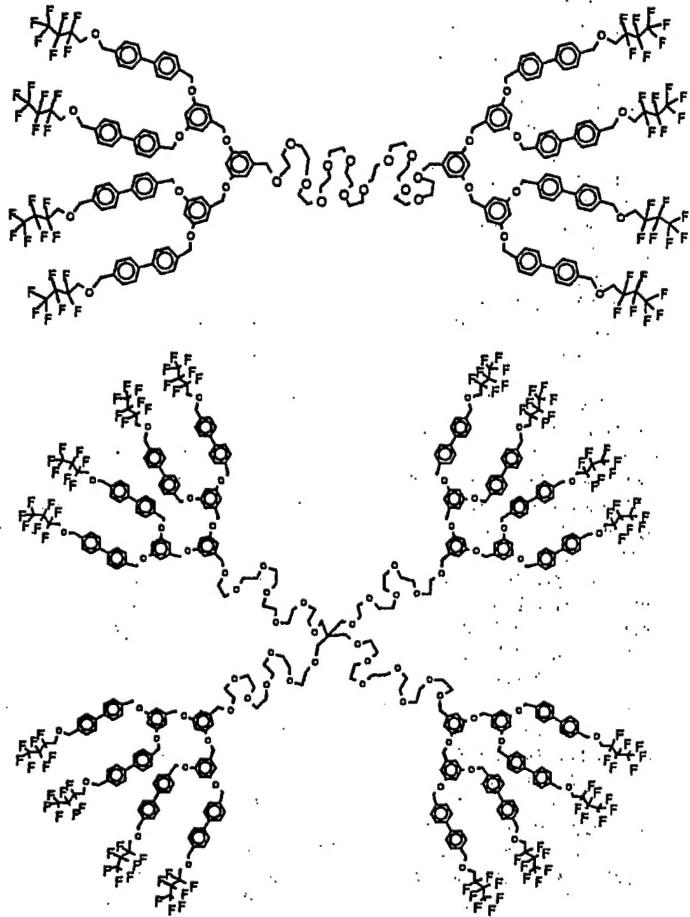


Figure 2. Copolymers of PEG or 4-arm star PEG and dendrimer with fluorinated alkyl chains.

Conclusion

Copolymers of PEG and analogs of second generation dendrimer have been synthesized and characterized. Normal polyether dendrimers can be replaced by other branched structures with similar physical properties. Incorporation of fluorinated chains enhance the hydrophobicity of the dendrimer. Attachment of long alkyl chains to dendrimers to achieve the same goal is under investigation and applications of the amphiphilic copolymers are being explored.

Acknowledgements

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